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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,067	ROTHENBERG ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-8, 19-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-18 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/26/04, 8/15/04*. + 1/9/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8 and 42-45 are drawn to an isolated CCR3 regulatory site comprising exon 1 of a human CCR3 gene, classified in class 536, subclass 24.1.

II. Claims 19-20 and 40 are drawn to an isolated CCR3 regulatory site comprising exon 2 of a human CCR3 gene classified in class 536, subclass 24.1.

III. Claims 25-26 and 41 are drawn to an isolated CCR3 regulatory site comprising exon 3 of a human CCR3 gene classified in class 536, subclass 24.1.

VI. Claims 31-34 are drawn to an isolated CCR3 regulatory site comprising a promoter of a human CCR3 gene, classified in class 536, subclass 24.1.

V. Claims 10-18 and 46 are drawn to a method for cell selective gene expression in a human by providing a pharmaceutically acceptable

formulation of at least one regulatory element capable of binding to an untranslated exon wherein said element regulates transcription of exon 1 in a human cell containing a CCR3 gene or mRNA, classified in class 514, subclass 44.

VI. Claims 10-14, 21-24 and 46 are drawn to a method for cell selective gene expression in a human by providing a pharmaceutically acceptable formulation of at least one regulatory element capable of binding to an untranslated exon wherein said element regulates transcription of exon 2 in a human cell containing a CCR3 gene or mRNA, classified in class 514, subclass 44.

VII. Claims 10-14, 27-30 and 46 are drawn to a method for cell selective gene expression in a human by providing a pharmaceutically acceptable formulation of at least one regulatory element capable of binding to an untranslated exon wherein said element regulates transcription of exon 3 in a human cell containing a CCR3 gene or mRNA, classified in class 514, subclass 44.

VIII. Claims 36-39 are drawn to a method for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein

said element regulates transcription of exon 1, classified in class 514, subclass 44.

IX. Claims 36-39 are drawn to a method for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exon 2, classified in class 514, subclass 44.

X. Claims 36-39 are drawn to a method for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exon 3, classified in class 514, subclass 44.

XI. Claims 36-39 are drawn to a method for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exon 4, classified in class 514, subclass 44.

2. Claim 9 link(s) the inventions groups V-VII. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 9. Claim 35 link(s) the inventions of groups VIII-XI. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 35. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 10-14 and 46 are generic to groups V-VI. Claims 36-39 are generic to groups VIII-XI. These claims will be examined limited to the groups elected. The inventions are distinct, each from the other because of the following reasons:

3. Inventions in groups I-IV and groups V-XI are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with

another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The inventions of groups I-IV are drawn to isolated regulatory sites of a human CCR3 gene. The inventions of groups V-XI are drawn to methods of regulating gene expression by binding of regulatory elements to a) untranslated CCR3 exons (groups V-VII) or b) a promoter in a human cell containing a CCR3 gene or mRNA. In the instant case, the inventions of group I-IV can all be used in a materially different process; i.e., hybridization assays for the detection of cell specific gene expression. Therefore, the inventions of groups I-IV are distinct from the inventions of groups V-XI.

4. Inventions of groups I-III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group I is drawn to an isolated CCR3 regulatory site comprising exon 1 of a human CCR3 gene. The invention of group II is drawn to an isolated CCR3 regulatory site comprising exon 2 of a human CCR3 gene. The invention of group III is drawn to an isolated CCR3 regulatory site comprising exon 3 of a human CCR3 gene. In the instant case the different inventions are not disclosed as capable of use together and will have different functions. The function of the invention of group I is to regulate the transcription of exon I, the function of the invention of group II is to regulate the transcription of exon 2 and the function of the invention of group III is

to regulate the transcription of exon 3. Therefore, the inventions of groups I-III are unrelated.

5. Inventions of groups I-III and group IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The inventions of groups I-III are described above. The invention of group IV is drawn to an isolated CCR3 regulatory site comprising a promoter of a human CCR3 gene. In the instant case the different inventions are not disclosed as capable of use together and will have different functions. The invention of group IV functions to enhance gene expression of the human CCR3 gene. The inventions of group I-III function to regulate the transcription of particular exons that comprise parts of the human CCR3 gene. Therefore, the inventions of groups I-III and IV are unrelated.

6. Inventions of groups V-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The invention of group V is drawn to a method for cell selective gene expression in a human by providing a pharmaceutically acceptable formulation of at least one regulatory element capable of binding to and regulating the transcription of exon 1 in a human cell containing a CCR3 gene or mRNA. The invention of group VI is drawn to a method for cell selective gene expression in a human by providing a

pharmaceutically acceptable formulation of at least one regulatory element capable of binding to and regulating the transcription of exon 2 in a human cell containing a CCR3 gene or mRNA. The invention of group VII is drawn to a method for cell selective gene expression in a human by providing a pharmaceutically acceptable formulation of at least one regulatory element capable of binding to and regulating transcription of exon 3 in a human cell containing a CCR3 gene or mRNA. In the instant case the different inventions are not disclosed as capable of use together and will have different functions. The function of the invention of group V is transcriptional regulation of exon 1, the function of the invention of group VI is transcriptional regulation of exon 2 and the function of the invention of group VII is the transcriptional regulation of exon 3. Therefore, the inventions of groups V-VII are unrelated.

7. Inventions of groups V-VII and groups VIII-XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The inventions of groups V-VII are described above. The inventions of group VIII-XI are drawn to methods for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of at least one of exon 1 (group VIII), exon 2 (group IX), exon 3 (group X) and exon 4 (group XI). In the instant case the different inventions are not disclosed as capable of use together and will have different functions. The inventions of groups V-VI

will function to provide a regulatory element capable of binding an untranslated exon sequence, thereby regulating the transcription of exons 1 through 3 respectively, of a cell containing a human CCR3 gene. The inventions of groups VIII-XI will function to provide a regulatory element capable of binding a promoter thereby regulating the transcription of exons 1 through 4 respectively, in a human cell containing a CCR3 gene or mRNA. Therefore, the inventions of groups V-VII and VIII-XI are unrelated.

8. Inventions of groups VIII-XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The inventions of groups VIII-XI are drawn to methods for cell selective gene expression in a human comprising providing at least one regulatory element for binding to a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exons 1-4 respectively. In the instant case the different inventions are not disclosed as capable of use together and will have different functions. The invention of group VIII functions to provide a regulatory element that binds a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exon 1. The invention of group IX functions to provide a regulatory element that binds a promoter in a human cell containing a CCR3 gene or mRNA wherein said element regulates transcription of exon 2 etc... Therefore, the inventions of groups VIII-XI are unrelated.

9. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and would require divergent searches of literature databases placing an undue administrative burden on the examiner, restriction for examination purposes as indicated is proper.

10. Applicant's election with traverse in the reply filed on July 19, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

11. Claims 1-8 and 19-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 19, 2004.

12. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth below. Figures 2, 4 and 9 disclose nucleotide sequences greater than 10 nucleotides in length that lack corresponding sequence identifiers in the figures or in the brief descriptions of the drawings. Appropriate correction is required in response to this action.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-18 and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 9-14 and 46 are drawn to a method for cell selective gene expression in a human comprising providing a pharmaceutically acceptable formulation of at least one regulatory element for binding to an untranslated exon in a human cell containing a CCR3 gene or mRNA (claim 9) wherein said element regulates transcription of at least one of exon 1, exon 2 or exon 3 (claim 10) wherein said element regulates binding of a transcription factor (claim 11) wherein said element is selected from a group consisting of a transcription factor inhibitor, an antisense oligonucleotide, and combinations thereof (claim 12) wherein said element is an inhibitor for a GATA transcription factor (claim 13) wherein the cell is selected from a group consisting of a leukocyte, an epithelial cell, an endothelial cell and combinations thereof (claim 14) that can also provide an agent selected from the group consisting of an antisense oligonucleotide against IL-5, a humanized anti-IL-5 antibody and combinations thereof (claim 46). Claims 15-18 are

drawn to a method of regulating expression of CCR3 comprising providing an inhibitor for a CCR3 exon 1 transcription factor to a human cell containing a CCR3 receptor (claim 15) wherein said inhibitor binds to CCR3 exon 1 at a GATA binding site (claim 16) that comprises SEQ ID NO: 16 (claim 17) or at least one of SEQ ID NO: 17, 18 or 19 (claim 18). "Cell selective gene expression" is not defined in the specification and is interpreted in the context of claims 9-14 and 46 to mean a method for regulating cell specific gene expression.

All of the above claims read broadly on one or more genera of biological molecules that are that are to be used in a method of treatment that functions through "cell selective gene expression". The genera are outlined below. In the instant case, claim 9 recites, "regulatory element for binding to an untranslated exon in a human cell." Claim 10 recites, "wherein said element regulates transcription of at least one of exon 1, exon 2 and exon 3." Claim 11 recites, "wherein said element regulates binding of a transcription factor." Claim 12 recites, "wherein said element is selected from the group consisting of a transcription factor inhibitor, an antisense oligonucleotide, and combinations thereof." Claim 13 recites, "wherein said element is an inhibitor for a GATA transcription factor." Claim 46 recites "an antisense oligonucleotide against IL-5, a humanized anti-IL-5 antibody and combinations thereof." Claim 15 recites, "an inhibitor for a CCR3 exon 1 transcription factor." Claim 16 recites, "wherein the inhibitor binds to a CCR3 exon 1 at a GATA binding site."

These claims encompass all regulatory elements and all untranslated human exons (claim 9), any human exon 1, 2 and 3 of any gene (claim 10), any transcription

factor (claims 11), any transcription factor inhibitor and any antisense oligonucleotides (claim 12) and any inhibitors for a GATA transcription factor (claim 13), any antisense oligonucleotide against IL-5 and any humanized anti-IL-5 antibody (claim 46), any inhibitors for CCR3 exon 1 transcription factors that binds at a GATA binding site (claims 15-16).

The specification discloses nucleotide sequences (exons of CCR3) and functional characterization of said sequences including demonstration of promoter activity in untranslated exon 1 by expression assay using deletion constructs and competitive binding assays. These results provide the informational starting point for a series of experiments that could be performed to fully characterize the functional role of the disclosed nucleotide sequence on CCR3 expression and the effects of this function in cells and organisms thereby providing the informational basis for a further series of experiments that could determine what particular compounds, drawn from broad genera of compounds, would be required to provide a method of treatment as claimed. Thus, applicant has only provided an invitation for further experimentation.

The specification discloses limited examples of the above genera of compounds that could function in the method as claimed. The disclosures of the specification are as follows. The specification discloses "regions containing regulatory sites at which regulatory elements may be blocked, for example, by inhibitors for one or more transcription factors that bind to the gene in that region" (pg. 5). The specification does not disclose what these "regulatory elements" are or provide any examples of "regulatory elements." The specification discloses the structure (nucleotide sequence)

of several species of "untranslated exon" that are "exon 1, exon 2 and exon 3" from only a single human gene (CCR3). The specification discloses regions of nucleotide sequence that "contain binding sites for transcription factors, such as GATA-1, GATA-2, GATA-3, C/EBP and/or AML-1a" but does not disclose transcription factors that actually bind to these sites. The specification also discloses that "antisense oligonucleotides directed against exons 1, 2 or 3 will prevent mRNA accumulation" but does not disclose what these antisense oligonucleotides are. The specification discloses anti-GATA-1, 2 and 3 antibodies that are species of "inhibitors of transcription factors," "inhibitors for a CCR3 exon 1 transcription factor," and "inhibitors for a CCR3 exon 1 transcription factor that bind a GATA-1 site". The specification discloses a role for IL-5 in human disease and a single species of humanized monoclonal anti-IL-5 antibody that was used by others to treat disease. The specification does not disclose or provide any examples of IL-5 antisense oligonucleotides.

Therefore, no adequate written description for any of the above claimed genera of biological compounds/molecules is provided. Applicant provides no evidence for any shared distinguishing identifying characteristics of any of the disclosed species that would be a shared and defining characteristic for the genus. No structure is provided of any species disclosed within the scope of the claimed genera that corresponds with the function of any of these compounds in the method as claimed; i.e., that would be a structure required for performing said function.

To provide evidence of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered

include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In the instant case, what is the structure of a "regulatory element for binding to an untranslated exon," "exon 1, exon 2 and exon 3," "a transcription factor," "a transcription factor inhibitor," "an antisense oligonucleotide," "an inhibitor for a GATA transcription factor," "an antisense oligonucleotide against IL-5," a humanized anti-IL-5 antibody," or "an inhibitor for a CCR3 exon 1 transcription factor that binds a GATA binding site," for example?

Claim 14 recites, "wherein the cell is selected from a group consisting of a leukocyte, an epithelial cell, an endothelial cell and combinations thereof." This claim reads broadly on any human leukocyte, epithelial cell or endothelial cell. The specification discloses examples of cell types that are included in the genera of leukocytes, epithelial cells and endothelial cells (pg. 9). However, the specification does not provide sufficient distinguishing identifying characteristics for each of the genera of cells claimed such that it is clear that applicant was in possession of said genera. Applicant has not described what distinguishing identifying characteristics define all epithelial cells that can be treated with the method as claimed, for example?

Vas-Cath Inc. v. Mahurkar, 19USPQ2nd 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed (see page 1117). The

specification does not "clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." (see *Vas-Cath*, pg 1116). In the instant case, the skilled artisan cannot envision an exact structure for any of the multiple genera of biological molecules as claimed and outlined above wherein said genera include regulatory elements, untranslated exons, human exons 1, 2 and 3, transcription factors, inhibitors of transcription factors, antisense oligonucleotides, inhibitors of GATA transcription factors, inhibitors for a CCR3 exon 1 transcription factor that can bind at a GATA site. Additionally, the skilled artisan cannot envision the distinguishing identifying characteristics for each of the genera of cells that are leukocytes, endothelial cells or epithelial cells. Adequate written description for the invention as claimed requires more than statements that disclose a single species of the invention when the claims are drawn to the entire genus.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 20 USPQ2s 1481 at 1483. In *Fiddes*, claims directed to mammalian FGS's were found to be unpatentable due to lack of written description for that broad class. The specification provided only bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see pg 1115).

Therefore, applicant has not provided an adequate written description of the invention and the manner and process of making and using said invention such that one skilled in the art would be able to make and use the same.

14. Claims 9-18 and 46 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the specification does not enable a treatment that is a method for cell selective gene expression in a whole human (which embraces a method of regulating expression of CCR3 in a human cell).

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

Claims 9-18 and 46 are drawn to a method for cell selective gene expression, the full breadth of which is described above. Each of these claims reads broadly on a method of treatment. The specification, however, provides no support for a method of treatment. There is no disclosure that would allow the skilled artisan to envision what specific compounds would be required to practice the instant invention that would be embraced by the metes and bounds of a treatment that is a method of cell selective gene expression. The specification discloses nucleotide sequences (exons of CCR3) and functional characterization of said sequences including demonstration of promoter

activity in untranslated exon 1 by expression assay using deletion constructs and the potential for transcription factors to bind said sequences using competitive binding assays. These results provide the informational starting point for a series of experiments that could be performed to fully characterize the functional role of the disclosed nucleotide sequence on CCR3 expression and the effects of this function in cells and organisms thereby providing the informational basis for a further series of experiments that could determine what particular compounds, drawn from broad genera of compounds, would be required to provide a method of treatment as claimed. Therefore, applicant has only provided an invitation for further experimentation, since the specification is merely prophetic and provides no guidance for determining how the skilled artisan would practice the method of treatment as claimed.

The breadth of the claims is so broad that one skilled in the art, in order to make and use the invention as claimed, would be required to carry out an undue quantity of experimentation to determine what specific biological compounds from the undefined genera as claimed, will function in the method as claimed. To practice the method of the instant invention, one skilled in the art would have to determine which of any of a broadly drawn class of biological compounds known as "regulatory elements" (that could be "a transcription factor inhibitor, an antisense oligonucleotide or combinations thereof" or could be "an inhibitor for a GATA transcription factor) for binding to any of another broadly drawn class of biological compounds known as "untranslated exons" could regulate the expression of at least one of any human "exon 1, exon 2 and exon 3" or could regulate binding of a transcription factor.

The state of the prior art at the time of filing recognizes broad classes of compounds that are grouped by the functional effect on gene expression termed regulatory elements (that includes at least cations, antibodies, small molecule inhibitors, antisense oligonucleotides, DNA binding proteins) and transcription factors (including multiple unrelated proteins). The state of the prior art at the time of filing also recognizes "untranslated exons" from minor transcripts of a small subset of human genes but does not provide significant teaching concerning untranslated exons other than indicating that these exons are not well characterized or well known. This is exemplified by Roberts et al. 2001 who detail the discovery of a minor transcript of the human ALAS1 gene that contains an additional exon in the 5' region (pp. 102-103).

There is a high degree of unpredictability in the art of providing a treatment for a disease via the function of cell selective gene expression. The method of treatment as claimed relies on a regulatory element binding an untranslated exon and will function, at a minimum, only where the particularly targeted untranslated exon modulates transcription and is included in a cell selective mRNA transcript variant. There is no way of predicting, *a priori*, to what genes the above will apply because all genes and all transcriptional signals of those genes are not known. Two individuals performing a method of cell selective gene expression by providing an undefined regulatory element that binds to any untranslated exon in a human would not be able to predict, *a priori*, which, of all the human genes can be modulated in a method of treatment or in what cells this method might be practiced.

Additionally, although particular species of biological compounds from within the genera claimed that would be necessary to practice the method of treatment as claimed can be obtained by a series of individual protocols, all of which are known to one skilled in the art, the more or less standard nature of each type of experiment required in order to embrace the scope of the claimed invention is outweighed by the sheer quantity of experimentation that would be required. In order to practice this invention as claimed, the skilled artisan would have to perform a large quantity of experiments in order to determine *de novo* the structure and function of multiple, broadly drawn genera of biological compounds (see above) that would function in the method as claimed. Additionally, there is no guarantee that after such experimentation, the identified compounds could be employed in a cell selective manner.

Therefore, based on the nature of the invention as a method of treatment, the degree of unpredictability in the art, the breadth of the claimed method, the limited guidance as to what particular species of compounds from within undefined genera of compounds would be required to practice the method as claimed, the need to screen multiple species of compounds from multiple undefined genera that would allow identification of particular species as functional within the method of treatment as claimed and the quantity of *de novo* experimentation necessary to discover the above, an undue amount of experimentation that would be required in order to practice the method of treatment as claimed. Therefore, the inventors have not enabled one skilled in the art perform the method of the claimed invention.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 recites, "at least one of exon 1, exon 2 and exon 3." In the instant case, the scope of what is claimed by "exon 1, exon 2 and exon 3" is indefinite, rendering claims drawn to this scope, indefinite. An "exon" is an art recognized term the scope of which is broadly drawn to mean the nucleotide sequences of the primary RNA transcript (or the DNA that encodes them) that exit the nucleus as part of a messenger RNA molecule. The terms "exon 1, exon 2 and exon 3", however, are directed to particular exons of particular genes that are not identified. Applicant has disclosed a single example of a single exon 1 exon 2 and exon 3 from a single human gene (CCR3). Applicant, however, has not defined the meaning of an "exon 1, exon 2 and exon 3" in the specification such that a person of ordinary skill in the art would be apprised of the metes and bounds of what is encompassed by the instant claims. What exon 1, exon 2 and exon 3 of the thousands of human exons designated exon 1 or exon 2 or exon 3, from thousands of human genes, are being claimed, for example? The specification as filed provides no clear definition or clear guidance as to the meaning of "exon 1, exon 2 and exon 3." Therefore, because the scope of claim 10 cannot be determined, claim 10 is rejected as being indefinite.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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